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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,662	01/03/2008	Giuseppe Alvaro	PB60564USW	4280

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EXAMINER	
CHANG, CELIA C	
ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
02/01/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/595,662	ALVARO ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *23 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-44* is/are pending in the application.

4a) Of the above claim(s) *32-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-24, 29* is/are rejected.

7)☒ Claim(s) *25-28,30 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

1. Applicant's election without traverse of group I, claims 17, 22, 23-27 and claims 16, 18-21, 29-31 wherein n=2 in the reply filed on Nov. 23, 2010 is acknowledged.

Claims 1-15 have been canceled.

Claims 17, 22, 23-28 and claims 16, 18-21, 29-31 wherein n=2 are prosecuted.

Claims 32-37 and newly added claims 38-44 are withdrawn form consideration.

Please note that claims 38-44 were newly added which would be restrictable were they presented in the previous claim sets because hydrates/solvates of a specific compounds with particular crystalline properties have been set forth by artisan in the field to be different chemical identity (see Seddon) and in possession of one would not have any prediction of another (see Braga p.3640).

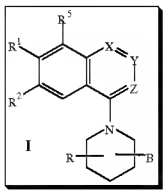
2. Claims 16-22 and 23-24, 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompassed the scope of "solvates of the compounds" for which no description or enabling support can be found in the specification. Please note that each solvate is a different "chemical identity" and there should never be any doubt in this century as to the chemical identity of a material (see Seddon). Unlike formation of salts between a pharmaceutically acceptable acid and an organic base compound of the claims, the formation of "solvates" must find descriptive and enabling support for such claimed scope because absent of specific description, one having ordinary skill in possession of compounds would not be able to offer any predictability of which one will form what solvate (see Braga p.3640). A survey of the specification indicated there is no description of which solvent can form solvate with the compounds, under what condition will such solvates be obtained, and whether the solvates will have consistent properties to be considered inclusive as being a "Markush" alternative of the compounds.

No examples, no process of making, no starting material or operability can be found for any compound encompassed by the Markush formula to have the ability in forming what solvate. Therefore, absent of description and enabling disclosure, the specification is insufficient in supporting the "claimed" scope of "solvates of the compounds".

The above factors, regarding the present invention, are summarized as follows:

(a) Breadth of the claims - the breadth of the claims includes all of the tens of thousands of piperidinyl-substituted pyrrolidones and pharmaceutical compositions of the formula I, as well as the myriad of potential salts and solvates formulated from these of piperidinyl-substituted pyrrolidones and pharmaceutical compositions of the formula I, respectively;



(b) Nature of the invention - the nature of the invention is evaluation of solvates and of piperidinyl-substituted pyrrolidones and pharmaceutical compositions of the formula I and the pharmacokinetic behavior of these substances in the human body as agents for the treatment of psychiatric disorders and as NK1 antagonists, seretonin transporter inhibitors or serotonin reuptake inhibitors;

(c) State of the prior art - Nature Reviews: Drug Discovery offers a snapshot of the state of the drug development art. Herein, drug development is stated to follow the widely accepted Ehrlich model which includes: 1) development of a broad synthetic organic chemistry program; 2) subsequent testing of compounds in an appropriate laboratory model for the disease to be treated; and 3) screening of compounds with low toxicity in prospective clinical trials (Jordan, V. C. Nature Reviews: Drug Discovery, 2, **2003**, p. 205);

(d) Level of one of ordinary skill in the art - the artisans synthesizing applicant's compounds, salts or solvates of piperidinyl-substituted pyrrolidones and pharmaceutical compositions of the formula I, would be a collaborative team of synthetic chemists and/or health practitioners, possessing commensurate degree level and/or skill in the art, as well as several years of professional experience;

(e) Level of predictability in the art - Synthetic organic chemistry is quite unpredictable (In re Marzocchi and Horton 169 USPQ at 367 ¶ 3). The following excerpt is taken from Vippagunta, et al. with respect to the synthesis of solvates of piperidinyl-substituted quinazolines and pharmaceutical compositions of the formula I (Vippagunta, et al. Advanced Drug Delivery Reviews, 48, **2001**, p. 18):

Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible

formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates.

(f) Amount of direction provided by the inventor - the application is negligent regarding direction with respect to making and using solvates of all kind of piperidinyl-substituted pyrrolidones and pharmaceutical compositions of the formula I;

(g) Existence of working examples - applicant has provided sufficient guidance to make and use piperidinyl-substituted pyrrolidones and pharmaceutical compositions of the formula I and pharmaceutically addition salt; however, the disclosure is insufficient to allow extrapolation of the limited examples to enable the scope of the tens of thousands of solvates/hydrates of piperidinyl-substituted pyrrolidones or solvates/hydrates of all salts of piperidine substituted pyrrolidones and pharmaceutical compositions of the formula I. The specification lacks working examples of solvates/hydrates of all kinds for piperidinyl-substituted pyrrolidones and pharmaceutical compositions of the formula I.

Please note that the specification provided exclusively only compounds wherein R is 4-fluorophenyl (scope of claim 18), R5 is optionally substituted phenyl or naphthyl, and n=2 compounds having the claimed utility (see biological data p.38-39) and among the thousands of compounds and salt only two salts are crystalline (1-[(3,5-Dichlorophenyl)methyl]-3-[4-(4-fluorophenyl)-4-piperidinyl]-l,5-dihydro-2H-pyrrol-2-one fumarate and citrate) and one hydrate of the citrate salt.

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. Markush claims must be provided with support in the disclosure for each member of the Markush group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP § 608.01(p).

(h) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

- predicting whether a recited compound is in fact one that produces a desired physiological effect at a therapeutic concentration and with useful kinetics, is filled with experimental uncertainty, and without proper guidance, would involve a substantial amount of experimentation (Jordan, V. C. Nature Reviews: Drug Discovery, 2, **2003**, pp. 205-213).

-predicting whether a recited compound can form solvate when in possession of the compound per se is in fact a nightmare (see Braga p.3640).

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. {In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)}.

3. Claims 25-28, 30-31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Jan. 24, 2011

/Celia Chang/
Primary Examiner
Art Unit 1625